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Association between the 15-kDa selenoprotein and UDP-glucose:glycoprotein glucosyltransferase in the endoplasmic reticulum of mammalian cells.

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Mammalian selenocysteine-containing proteins characterized with respect to function are involved in redox processes and exhibit distinct expression patterns and cellular locations. A recently identified 15-kDa selenoprotein (Sep15) has no homology to previously characterized proteins, and its function is not known. Here we report the intracellular localization and identification of a binding partner for this selenoprotein which implicate Sep15 in the regulation of protein folding. The native Sep15 isolated from rat prostate and mouse liver occurred in a complex with a 150-kDa protein. The latter protein was identified as UDP-glucose:glycoprotein glucosyltransferase (UGTR), the endoplasmic reticulum (ER)-resident protein, which was previously shown to be involved in the quality control of protein folding. UGTR functions by glucosylating misfolded proteins, retaining them in the ER until they are correctly folded or transferring them to degradation pathways. To determine the intracellular localization of Sep15, we expressed a green fluorescent protein-Sep15 fusion protein in CV-1 cells, and this protein was localized to the ER and possibly other perinuclear compartments. We determined that Sep15 contained the N-terminal signal peptide that was essential for translocation and that it was cleaved in the mature protein. However, C-terminal sequences of Sep15 were not involved in trafficking and retention of Sep15. The data suggest that the association between Sep15 and UGTR is responsible for maintaining the selenoprotein in the ER. This report provides the first example of the ER-resident selenoprotein and suggests a possible role of the trace element selenium in the quality control of protein folding.

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[Redox reactions of Sep15 and its relationship with tumor development]

[Article in Chinese]

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BACKGROUND & OBJECTIVE: Sep15 is a selenium-containing protein identified in 1998. This protein may be involved in cancer etiology and it may have redox function. The objective of this study was to investigate the relationship between the redox function of Sep15 and tumor development. METHODS: The full-length DNA sequence of Sep15 was obtained by RT-PCR and then recombined to eukaryotic expression vector pcDNA3.1(+). The BEL-7402- Sep15 cell line, which expressed the high levels of Sep15 by transfecting the cultured hepatocarcinoma cell line BEL-7402 with pcDNA3.1-Sep15 was generated. From morphologic investigation, cell growth curve, clone formation and nude mice tumor growth curve, the relationship between Sep15 and hepatocarcinoma cell line BEL-7402 was determined. Furthermore, the redox reaction of sep15 was detected by MTT assay. RESULTS: There was no distinct effect of transfection of Sep15 gene on BEL-7402-Sep15 cell. The cell survival rate was drastically different between BEL-7402-Sep15 cell and both BEL-7402- pcDNA cell and BEL-7402-Sep15 cell after foreign H2O2 reactive oxygen stress ($P<0.05$). CONCLUSION: Transfecting Sep15 gene did not influence the growth characteristics of BEL-7402 cell line and Sep15 may have redox function.

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